Summary of Safety and Effectiveness

Beta-2-Microglobulin Method for Bayer Technicon Immuno 1® System

1. Intended Use

This is an *in vitro*, solid-phase enzyme immunoassay for the quantitative measurement of beta-2-Microglobulin in serum and urine. Measurements of beta-2-Microglobulin are used in monitoring inflammatory conditions and in diagnosing and managing patients with renal diseases.

Listed below is a comparison of the performance between the Immuno 1 beta-2-Microglobulin method and a similar device that was granted FDA clearance of substantial equivalence (The Abbott IMX beta-2-Microglobulin Assay). The information used in this Summary of Safety and Effectiveness was extracted from the Immuno 1® beta-2-Microglobulin method sheet, from data on file at Bayer Corporation, and from the Abbottt IMX beta-2-Microglobulin method sheet.

METHOD	Immuno 1 beta 2-Microglobulin		Abbott IMX (predicate D	
Part No.	Reagents Calibrators	T01-3669-51 T03-3670-01	2201-20	
Minimum Detectable Conc.	0.01 mg/L		0.005 mg/L	
Precision (within-run)	SERUM 1.48 mg/L 2.57 mg/L 9.8 mg/L URINE 0.13 mg/L 0.91 mg/L 13.56 mg/L	1.25% 1.89% 1.48% 1.10%	SERUM 1.7 mg/L 3.9 mg/L 9.7 mg/L URINE 0.10 mg/L 0.30 mg/L 0.89 mg/L	6.0% 4.4% 4.9% 4.7% 5.5% 4.8%
Correlation	SERUM y=0.99x+0.11 where y=Immuno 1 x= Abbott IM n=97 r=0.99 Syx=0.93 mg/s		URINE y=1.05x-0.05 where y=Immuno x=Abbott IM n=24 r=0.99 Syx=0.52 mg	x

2. Assay Description

sample. A cubic fit through zero is used to calculate the dose response curve. obtained response is directly proportional to the concentration of beta-2-Microglobulin in the nitrophenolphosphate is added as the enzyme substrate. The increase in absorbance due to the the mIMP reagent is added and the complex is captured by the anti-fluorescein antibodies on the Microglobulin--ALP-conjugate complex is formed. After 14 minutes of incubation an aliquot of Six calibrators with beta-2-Microglobulin concentrations of 0, 0.4, 0.85, 3.0, 8.0 and 20.0 mg/L formation of p-nitrophenolate is monitored spectrophotometrically at 405 nm and 450 nm. The magnetic particles. The particles are precipitated by an external magnetic field, washed and paraincubated at 37 °C. In the presence of beta-2-Microglobulin a fluorescein-conjugate--beta-2-(mIMP reagent). Sample or calibrator, R1 and R2 reagent are mixed simultaneously and phase consists of a suspension of magnetizable particles coated with antibody to fluorescein fluorescein (R1) and the polyclonal antibody labelled with alkaline phosphatase (R2). The solid capture and a polyclonal (sheep) detector antibody. The monoclonal antibody is labelled with Beta-2-Microglobulin is an enzyme label sandwich immuno-assay using a monoclonal (mouse)

3. Imprecision

a) Serum Samples

curve genrated on day 1 of the study. (Table 1) Immuno 1 over 10 days. The concentrations of serum controls were calculated from a calibration Imprecision data for serum samples was obtained by analyzing human serum controls on an

Table 1

specimen	Mean (mg/l)	Total SD (mg/l)	Total CV (%)	Within-Run SD (mg/l)	Within-Run CV (%)
sample 1	1.48	0.033	2.25	0.026	1.79
sample 2	2,57	0.039	***	0.032	1.25
sample 3	9,80	0.276	2.82	0.185	1.89
sample 4	0.27	0.005	1.89	0.005	1.85
sample 5	and a supplementation of the supplementation	0.019	1.61	0.017	1,45
sample 6	3.51	0.072	2,05	0.072	2.05
sample 7	5.78	0.152	2.63	0.139	2.41
sample 8	11.06	0.325	2.93	0.254	2.30
sample 9	15.81	0.445	2.81	0.400	2.53

b) Urine Samples

Imprecision data for urine samples was obtained by analyzing human urine controls on an Immuno 1 over 5 days. The concentrations of serum controls were calculated from a calibration curve genrated on day 1 of the study. (Table 2)

Table 2

specimen	Mean (mg/l)	Total SD (mg/l)	Total CV (%)	Within-Run SD (mg/l)	Within- Run CV (%)
sample 1	0.13	0.005	3.46	0.002	1.48
sample 2	0.91	0.012		0.010	1.10
sample 3	13.56	0.676	4.98	0.676	4.98

4. Correlation

a) Serum Samples

A total of 97 serum samples were tested on the Abbott IMx (x) and the Immuno 1 (y). The correlation results are shown in Figure 1.

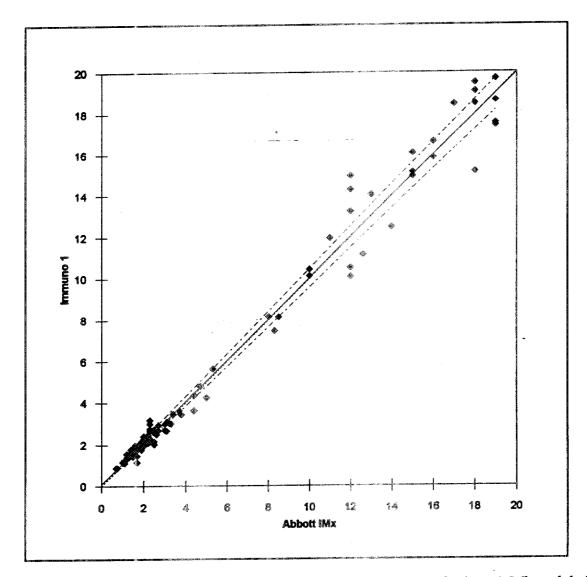


Fig 1: Serum Sample Correlation of Immuno 1 vs. Abbott IMX for beta-2-Microglobulin The correlation equation according to Bablok-Passing was

$$y = 0.99 x + 0.11$$

 $r = 0.9917$
 $Syx = 0.93 mg/L$

b. Urine Samples

A total of 24 urine samples were tested on the Abbott IMx (x) and the Immuno 1 (y). The correlation results are shown in Figure 2.

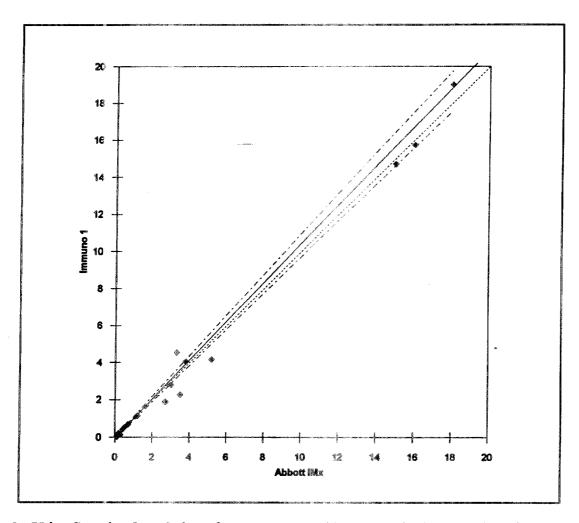


Fig 2: Urine Samples Correlation of Immuno 1 vs. Abbott IMX for beta-2-Microglobulin

The correlation equation according to Bablok-Passing was

$$y = 1.05 \times -0.05$$

 $r = 0.9956$
 $Syx = 0.52 \text{ mg/L}$

5. Interferences

For all interference measurements, a pool was spiked with potentially interfering substances and cross-titered against an identical pool containing no interferants. Beta-2-Microglobulin recoveries for interference pools are summarized in Table 3.

Table 3

incriennis sage	Interferant	B2-M Recovery
	Conc (mg/dL)	2.56
Alburnin	1625	2.58
Albuilli	3250	2.57
	4875	2.56
	6500	2.58
		2.53
Bilirubin	6.25	2.46
Sim won.	12.50	2.40
	18.75	2.45
	25	2.41
BELLEVICE OF THE STATE OF THE S	AND DESCRIPTION OF THE PROPERTY OF THE PROPERT	2.70
Urea	50	2.69
	100	2.69
	175	2.70
	200	2.56
to a contract with the contrac	Dans 17 Western 2 Inches processors Compared State Annual Compared September 1997 (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (1997) (199	2.61
Hemoglobin	300	2.60
	600	2.75
	800	2.63
	1200	2.69
and the state of t	0	2.64
Heparin	12.5	2.60
_	25	2.41
	37.5	2.56
	50	2.78
98	0	2.40
Human IgG	1325	2.50
_	2650	2.40
	39 7 5	2.50
	5300	2.54
	0	3.31
Triglycerides	250	3.36
	500	3.56
	750	3.56
Sur Section Control	1000	3.43

6. Sample Dilution

Serum and urine samples were diluted with beta-2-Microglobulin Calibrator Level 1 and with Sample Diluent B was carried out. For data analysis a linear regression was calculated from the results of undiluted, 10%, and 25% diluted pools. The expected results and the deviation from the measured values were calculated from this equation; these are shown in Tables 4-7.

I. Results obtained with Calibrator Level 1 as diluent

a) Serum Samples

Table 4

		Table 4	······································	
sampis	dilution (%)	cont. (mens.)	ecque (este)	deviation (%)
1	0	0	0.04	•
	10	1,19	1.12	5.6
anny specifylian a finishing septiment type statement a transport and a section of the section o	A STATE OF THE PROPERTY OF THE	2.72	2.75	-1.0
	50	5.39	5.45	-1.2
	The state of the s	8.62	8.16	5.3
and her the second seco	100	11.06	10.87	1.8
2	0	0	0.03	•
eng en susceptus en en en el responsable sem significación de la completa de la completa de la completa de la c	10	1.16	1.10	4.8
and the second of the second o	of the second se	2.69	2.71	-0.8
	50	5.01	5.39	-7.6
and the state of t	and S	8.65	8.07	6.7
	100	11.68	10.75	8.0
3		0	0.08	•
	10	1.62	1.49	8.0
		3.56	3.61	-1.4
manifestration of the second o	50	7.10	7.15	-0.6
	75	11.64	10.68	8.2
	100	14.39	14.21	1.2
4	0	0	0.02	•
elegy to the control of the control	10	1.05	1.02	2.6
		2.52	2.53	-0.4
	50	5.07	5.05	0.5
	The statement of the st	7.95	7.56	4.9
	100	11.06	10.07	8.9
5	0	0	0.04	•
ett ett tjätik ennikkirkot killin puittavia killi peet 1 kunt maatavi kunt / Põhill ^{in k} untavasuus heksilijä killin ki Ha	10	1.74	1.67	4.2
o conservence i grande and execute pe la plan i mana construción de la mana la mana la mana la mana la mana la	And the second section of the contract of the second secon	4.07	4.10	-0.7
	од се при	8.97	8.15	9.1
		V V		
ang a s ⁱ nda ang birth states pas P _{LIS} dang data states kentrock birth states pang birth si bir birth si birth s	A SECTION OF THE PROPERTY OF T	13.4	12.2	8.9
		13.4 17.11		8.9 4.9
6	A STATE OF THE STA	13.4 17.11 0	12.2 16.27 0.08	
	75 100	13.4 17.11	12.2 16.27 0.08 1.92	4.9 - 5.4
6	75 100 0	13.4 17.11 0	12.2 16.27 0.08	4.9
	75 100 0	13.4 17.11 0 2.03	12.2 16.27 0.08 1.92	4.9 - 5.4 -0.9 -8.9
	75 100 0 10 25	13.4 17.11 0 2.03 4.66	12.2 16.27 0.08 1.92 4.70	4.9 - 5.4 -0.9

b) Urine Samples

Table 5

sample	dilution (%)	conc. (meas.)	conc. (calc.)	deviation (%)
1	0	0	0	-
And the second of the second o	10	0.87	0.88	-0.8
	25	2.2	2.2	0
	50	4.33	4.40	-1.6
entering to the state of the st	75	6.76	6.60	2.4
	100	9.08	8.80	3.1
2	0	0	-0.3	-
water and a state of the state	10	1.64	1.69	-2.9
	ne proposition de la company d	4.28	4.26	0.4
er and the Market on one of the second of th	50	8.89	8.55	3.8
with the manufacture and 2 types are would find a major.	en enterprisonation protective delication of the restriction and an extended the restriction of the restrict	13.59	12.84	5.5
	100	17.34	17.13	1.2
3	0	0	0.03	•
age and great and definition of the large group and another the large group and the large group and the large g	10	1.13	1.09	3.84
	See S	2.66	2.68	-0.7
	450	4.82	5.33	-10.6
	and the second of the contract of the second	7.62	7.98	-4.7
	100	11.16	10.63	4.7
4	0	0	0.07	•
wy yn ymuw y 1877 i BAT GANCA (GWYyggy) y yn cygwyn i B A Affidd GWYR GWYn gynwyn o Babir . A Maldin	10	1.53	1.41	7.7
eninks operate in the second field the second contract of the second	25	3.38	3.43	as 1.4
	50	7.63	6.78	11.1
	75	11.23	10.14	9.7
ee agamaya dagbasaankii ilii ilii ilii kaassaa asaa asaa an mahka ilii ilii ilii ilii ilii aasaa aanaan sebahi	100	12.73	13.50	-6.0

II. Results obtained with Sample Diluent B

a) Serum Samples

Table 6

sample	dilution (%)	conc. (meas.)	conc. (calc.)	deviation (%)
1	0	0	-0.01	go.
	10	1.45	1.44	1.0
maker karandari epigengan andari hasi hiri 20 meneringan hali kecaman ana pada hiri daga menerin da i	25	3.57	3.58	-0.2
And the second state of the second se	50	7.07	7.14	-1.0
metic (a les francisco de la company proper risco como un collega proper como con como metidos que la la mar rese	Same And Annual Control of the Contr	10.48	10.71	-2.2
	100	13.15	14.28	-8.6
2	0	0	-0.01	· ea
juma ta kacamatanya na kaonje na rezuweni i soli ini ini ka kacamata dipinini ini ini ini ini ini ini ini ini	до при на при В при на при	1.11	1.14	<u>~</u> 2.5
unique de placification de la proposición de la material de la deservación de la material de la deservación de	25	2.88	2.87	0.4
inening (and review) was passed and an exercise prior for the large gaps and an all the latter construction of the latter constru	50	5.84	5.75	1.5
	195	8.25	8.64	-4.7
	100	11.76	11.53	2.0

b) Urine Samples

Table 7

sample	dilution (%)	conc. (measi)	conc. (calc.)	deviation (%)
1	0	0	0.03	data
	10	1.81	1.75	3.1
Angeles des la chemical de la la lace de lace de la lace de lace de lace de lace de la lace de l	The and	4.31	4.33	-0.5
	50	8.64	8.63	0.1
	75	13.12	12.93	1.4
	100	16.92	17.22	-1.8
2	0	0	0.03	1300
and the second s	одина в одника од однога е ста постира и постира од	2.04	2.00	2.2
	25	4.93	4.95	-0.4
0,000	50	9.94	9.87	0.7
	The state of the s	15.51	14.79	4.6
	100	19.31	19.71	-2.1

7. Hook Effect

A serum sample with a concentration of 126 mg/l was diluted with calibrator level 1 and the rate values and calculated concentrations were compared to L6 calibrators. It can be concluded that even very high samples do not fall back into the assay range. (Fig. 3)

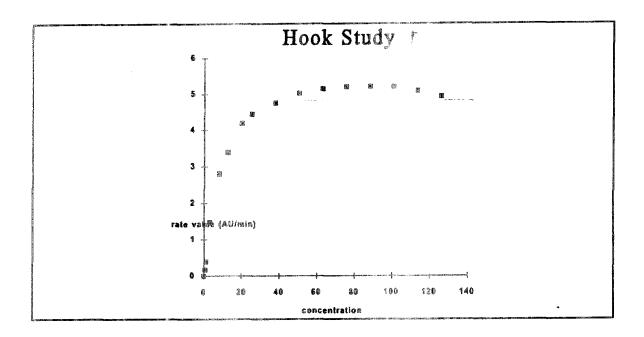


Fig. 3:

8. Recovery

Known amounts of beta-2-microglobulin were spiked into two serum and one urine samples. The recoveries cover a range of 92.5 % to 106 % are shown in Tables 8 and 9.

I. Serum Samples

	וח	

cone (calculated)	conc (measured)	recovery (%)
2.32	2.32	100
4.07	4.12	101.2
and the second s	The state and the state of the contract of the state of t	102.0
manufacture of management and manage	THE RESIDENCE PROPERTY AND ASSOCIATION OF THE PROPERTY ASSOCIA	103.2
nonempty subditions in temperature and the subject of the subject	and the contract of the contr	94.0
9.55	9,89	103.6
2.29	2.29	100
et granitas con la recorrecta de la contracta	44,00	98.5
TO DESCRIPTION OF THE PROPERTY	Managamentarian (*) 118 av da *) 118 av da *	98.0
and the second s	months of the state of the sta	96.8
and the latter was the latter to the latter	engated uses en inglesev, risk on 'n his no durante durante en konstenda samen sent stem et de l'accessé describé annue en l'accessé de	92.5
	9.67	101.4
	4.07 5.44 6.81 8.18	2.32 2.32 4.07 4.12 5.44 5.55 6.81 7.03 8.18 7.69 9.55 9.89 2.29 2.29 4.06 4.00 5.43 5.32 6.80 6.58 8.17 7.56

II. Urine Samples

Table 9

sample	conc. (calculated)	conc. (measured)	recovery (%)
sample 1 base	0.1	0.04	600
low	1.90	2. 18	114.7
low-mid	3.80	THE RESIDENCE AND THE PARTY OF	98.4
mid	and the suppression is the suppression and the	5.66	99.3
	7 60	от 63	100.4
high-mid	and a street of the street of	о по менения при выполня на при на п	100.8
high	9.50	7.20	100.0

9. Expected Values

I. Serum Samples

Serum samples from 262 healthy individuals were measured and gave the distribution of results shown in Fig. 4.

95 % of these serum samples were found to have concentrations of 2.15 mg/L or less. The calculated mean of this distribution is 1.35 mg/L, the median is 1.28 mg/L.

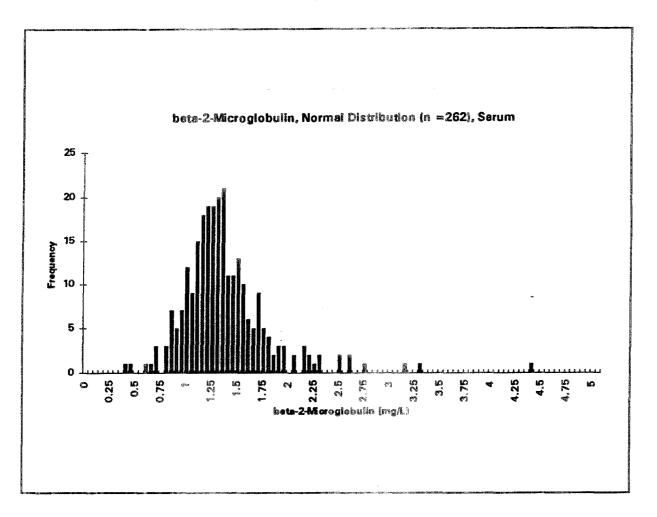


Fig. 4: Normal Distribution of beta-2-Microglobulin in Serum Samples

II. Urine Samples

Urine samples from 72 healthy individuals were measured; 95 % of these urine samples were found to have concentrations of 0.2 mg/L or less. The calculated mean of this distribution is 0.07 mg/L, the median is 0.04 mg/L. The distribution of results are shown in Fig. 5.

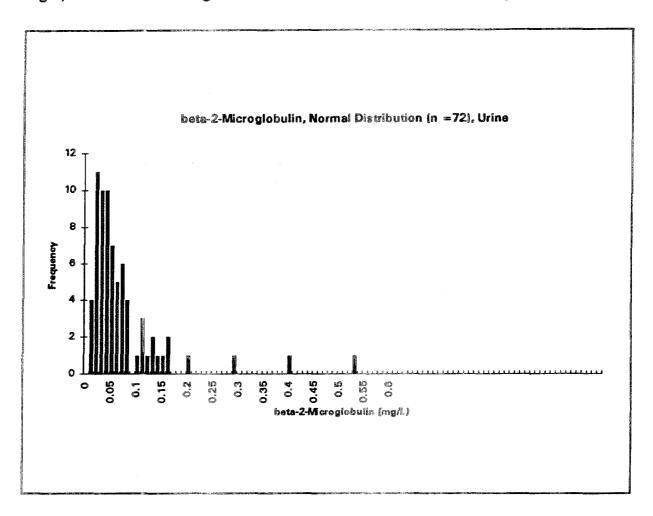


Fig. 5: Normal Distribution of beta-2-Microglobulin in Urine Samples

10. Minimum Detectable Concentration

Sensitivity or Minimum Detectable Concentration of the assay is defined as the beta-2-Microglobulin concentration that can be statistically distinguished for the zero calibrator – the mean zero absorbance + 2SD. The sensitivity measured in 32 seprate runs using 2 different lots of reagents and calibrators was determined to be 0.01 mg/L.





Food and Drug Administration 2098 Gaither Road Rockville MD 20850

MAY 2.9 1997

Mr. Gabriel J. Muraca, Jr. Manager Regulatory Affairs Bayer Corporation Diagnostics Division 511 Benedict Avenue Tarrytown, New York 10591

Re:

K964791/S1

Trade Name: \(\beta^2\) Microglobulin Assay for the Technicon Immuno 1\(\mathbb{B}\) System

Regulatory Class: II Product Code: JZG Dated: March 25, 1997 Received: March 26, 1997

Dear Mr. Muraca, Jr.:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Good Manufacturing Practice for Medical Devices: General (GMP) regulation (21 CFR Part 820) and that, through periodic GMP inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal Laws or Regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or at (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html"

Sincerely yours,

Steven I. Gutman, M.D., M.B.A.

Steven Butman

Director

Division of Clinical Laboratory Devices

Office of Device Evaluation

Center for Devices and Radiological Health

Enclosure

		$Page_{\underline{1}} of \underline{1}$
510(k) Nu	umber (if known): <u>K 96 4791</u>	NAMES OF THE STREET
Device Na	Tachnican Immuna 10 System 1	32-Microglobulin (B2S / B2U)
	s For Use:	• • • • • • • • • • • • • • • • • • •
,	This in vitro diagnostic method is intended concentration of β2-microglobulin in human 1® system. β2-Microglobule should be used in conjunction with inform other diagnostic procedures in the managedysfunction and rheumatoid arthritis.	nan serum and urine using the roglobulin assay values obtained nation available from clinical and
	This diagnostic method is not intended for	or use on any other system.
		Jeter & Maxim
		(Division Sign-Off) Division of Clinical Laboratory Devices 510(k) Number
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Prescription	on UseOR FR 801.109)	Over-The-Counter Use
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